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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/626,616 | 07/27/2000 | Lei Yu | INDA:005USD1 | 1049 |

7590 05/30/2002

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| EXAMINER |
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| ART UNIT | PAPER NUMBER |
|---|---|
| 1647 | 13 |

DATE MAILED: 05/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/626,616 | YU, LEI | |
| | Examiner | Art Unit | |
| | Robert Landsman | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *83-101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *83-90,92-99 and 101* is/are rejected.

7)☒ Claim(s) *91 and 100* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

*1. Formal Matters*

A. Amendment D, filed 2/26/02, has been entered into the record.

B. Supplemental Amendment E, filed 4/11/01, has been entered into the record.

C. Claims 44-47, 65-74 and 76-82 were pending in this application. However, these claims have been canceled in Supplemental Amendment E and new claims 83-101 have been added by this Supplemental Amendment. Therefore, claims 83-101 are pending in this application and are the subject of this Office Action.

D. In the Office Action, dated 7/17/01, part (d) of the "Formal Matters" stated that claim 44 included various distinct protein sequences and was subject to restriction. However, no restriction requirement was, in fact, made. Therefore, since these four opioid receptor sequences have already been searched, a restriction requirement will not be made.

E. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

*2. Oath/Declaration*

A. The Declaration of Lei Yu, filed 2/26/02, has been entered into the record. This Declaration replaces the original Declaration filed with the instant application and was filed to include parent Application No. 08/056,886, which was filed March 03, 1993. Application No.08/056,886 was not referenced in the original Declaration.

*3. Specification*

A. The specification is objected to since the title recites "Polynucleotide encoding mu opioid receptor," whereas the claims are drawn to processes for screening candidate substances for their ability to bind opioid receptors, including the mu opioid receptor. The title should be amended to recite, for example, "Methods of screening for substances which bind opioid receptors."

B. The specification is objected to since the continuing data in the first line of the specification (Amendment D, filed 2/26/02) refers to U.S. Application Serial No. 08/889,108 as a "file-wrapper continuation" of 08/305,518 and refers to U.S. Application Serial Nos. 08/305,518 and 08/120,601 as "continuing applications." All of these applications must be referred to as either a "divisional" (DIV),

"continuation" (CON) or "continuation-in-part" (CIP). The records of the Office, as seen on the Bibliographic Data Sheet, show that 08/889,108 is a DIV of 08/305,518, that 08/305,518 is a CIP of 08/120,601 and that 08/120,601 is, itself, a CIP of 08/056,886.

C. The specification is further objected to since page 170 of the disclosure is missing.

*5. Claim Objections*

A. Claim 83 is objected to since part (b) of the claim is not necessary. It is obvious that a candidate substance would need to be obtained in order to be able to perform the claimed method of testing the candidate substance. Claims 84 and 85 are objected to since they depend from claim 83.

B. Claims 86 and 94 are objected to since the syntax could be improved by amending part (b) of the claims to recite "contacting the recombinant opioid polypeptide with the substance." Though the claim language, as recited by Applicant is not incorrect, usual perception in the art is that receptors (i.e. polypeptide) are normally contacted with substances, and not the opposite. This amendment will correspond to the terminology most commonly used in the art. It is also noted that claim 94 recites "candidate substance" in part (b) whereas claim 86 only recites "substance." Therefore, part (b) of claim 94 should be amended to include the appropriate terminology. Claims 87-93 and 95-101 are also objected to since they depend from claims 86 or 94.

C. Claims 86 and 94 are objected to since the syntax could be improved by inserting the word "for" between the words "encoded" and "by" in part (a). Claims 87-93 and 95-101 are also objected to since they depend from claims 86 or 94.

D. Claims 91 and 100 are objected to since they depend from rejected claims 86 and 94, respectively, for the reasons set forth in the below rejections under 35 USC, first and second paragraphs, but, themselves, are not rejected.

E. Claim 92 is objected to since the syntax could be improved by inserting the word "the" between the number "(ii)" and the word "ability." Furthermore, this claim recites two part "(ii)"'s. The second "(ii)" should be a "(iii)." This objection was made on page 4 of the Office Action dated 7/17/01 regarding

previous claim 72 – which corresponds to new claim 92. However, the Applicant did not address this issue.

*6. Claim Rejections - 35 USC § 112, first paragraph – written description*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. The rejection of previous claims 44-47 and 65-82 under 35 USC 112, first paragraph, on page 4 of the Office Action, dated 7/17/01, regarding the phrase "interacts with" has been withdrawn since these claims have been canceled and none of the new claims (83-101) recites "interacts with."

B. Claims 86-90, 92-99 and 101 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection was withdrawn in Paper No. 9 without a clear explanation on the record. However, upon further review, the Examiner reinstates these rejections.

These are genus claims. Claims 86-90 recite a process for screening a candidate substance for its ability to bind to a mu opioid receptor wherein the receptor is encoded for by a nucleic acid molecule comprising at least 35, 45, 50, 75, or 100 contiguous nucleotides of SEQ ID NO:7, including the guanine at position 389, by detecting the ability of the candidate substance to bind the opioid receptor polypeptide. Claim 93 recites the process of claim 86 wherein the opioid receptor is chimeric. Claims 94-99 recite a process for screening a candidate substance for its ability to bind to *any* opioid receptor wherein the receptor is encoded for by a nucleic acid molecule comprising at least 35, 45, 50, 75, or 100 contiguous nucleotides of SEQ ID NO:7, including the guanine at position 389, by detecting the ability of the candidate substance to bind the opioid receptor polypeptide. Claim 101 recites the process of claim 94 wherein the opioid receptor is chimeric.

However, the nucleic acid molecules encoding at least 35, 40, 45, 50, 75, or 100 contiguous nucleotides of SEQ ID NO:7, which are used in these screening methods, would have one or more nucleic acid substitutions, deletions, insertions and/or additions to the nucleic acid molecule of SEQ ID NO:7, and would encode for proteins with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:7.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. The Applicant is claiming a process for screening a compound its ability to bind opioid receptors. However, the Applicant has provided no written description as to what amino acid residues of these receptors are necessary in order to retain the ligand-binding characteristics of these opioid receptors (i.e. recitation of a binding domain), or as to what other residues are necessary to produce a functional opioid receptor. The protein encoded for by SEQ ID NO:7 (SEQ ID NO:8) is the only protein which has been described in the present specification which meets the limitations of claims 86-90, 92-99 and 101. Furthermore, the protein of SEQ ID NO:8 is 400 amino acid residues in length. However, the claims recite using polypeptides which encode as few as 12 amino acids of the protein of SEQ ID NO:8. Again, the Applicant has provided no written description as to what amino acid residues are necessary for ligands to bind to these opioid receptors, or as to what other residues are necessary to produce functional opioid receptors. These claims are reciting a process for screening opioid receptors (i.e. full-length receptors), and not for screening *fragments* of opioid receptors, which are encompassed by proteins encoded for by at least 35, 45, 50, 75, or 100 contiguous bases of SEQ ID NO:7. Apart from the length of the claimed polypeptides (35, 45, 50, 75, 100 bases), the only common structural attribute which identifies the members of the claimed genus of nucleic acid molecules and proteins is that they must comprise the guanine at position 389 of SEQ ID NO:7. Example VI, on page 121 of the specification discloses that the this guanine residue produces a 10-fold increase in affinity in dynorphin A (1-17) binding compared to the protein of Wang et al., which is encoded for by a nucleic acid molecule which does not comprise a guanine at position 389 of SEQ ID NO:7. However, the general knowledge and level of skill in the art do not supplement the omitted description of what amino acid residues are necessary to produce a functional opioid receptor because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "35, 45, 50, 75, or 100 contiguous bases of SEQ ID NO:7 including guanine 389" alone is insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made. Claim 92 is rejected since it depends from rejected claim 86.

*7. Claim Rejections - 35 USC § 112, first paragraph – lack of enablement*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 86-90, 92-99 and 101 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for screening a candidate substance for its ability to bind to an opioid receptor encoded for by a nucleic acid molecule comprising SEQ ID NO:7 in its entirety, as well as screening a candidate substance for its ability to bind to chimeric opioid receptors comprising SEQ ID NO:7 in its entirety, does not reasonably provide enablement for a process for screening a candidate substance for its ability to bind to an opioid receptor encoded for by a nucleic acid molecule comprising at least 35, 45, 50, 75, or 100 contiguous nucleotides of SEQ ID NO:7, including the guanine at position 389, nor does the specification provide enablement for screening a candidate substance for its ability to bind to chimeric opioid receptors comprising said contiguous nucleotides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. This rejection was withdrawn in Paper No. 9 without a clear explanation on the record. However, upon further review, the Examiner reinstates these rejections.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to screening a candidate substance for its ability to bind to an opioid receptor encoded for by a nucleic acid molecule comprising at least 35, 45, 50, 75, or 100 contiguous nucleotides of SEQ ID NO:7, including the guanine at position 389 as well as to screening a candidate substance for its ability to bind to chimeric opioid receptors comprising said contiguous nucleotides. Nucleic acid molecules comprising as few as 35 contiguous bases of SEQ ID NO:7 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to said polynucleotides. Similarly, the proteins encoded for by these nucleic acid molecules would encode for proteins with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:7.

Other than that encoded for by SEQ ID NO:7, Applicants provide no guidance or working examples of opioid receptor which are encoded for by as few as 35 contiguous bases of SEQ ID NO:7, nor is it predictable to one of ordinary skill in the art how to make a functional opioid receptor given that the receptor only needs to comprise anywhere from 11-33 contiguous amino acids of SEQ ID NO:8 (i.e. 35-100 contiguous bases of SEQ ID NO:7). Furthermore, claim 86 recites a process for screening a candidate compound for its ability to bind a mu opioid receptor, whereas claim 94 recites a process for screening a candidate compound for its ability to bind *any* opioid receptor. Again, the only guidance that the Applicant has provided in making an opioid receptor for use in the claimed screening process is that it must be encoded for by at least 35 contiguous bases of SEQ ID NO:7. Not only has the Applicant not taught the artisan how to make a functional *mu* opioid receptor encoded for by less than the full-length of SEQ ID NO:7 (claim 86), but the Applicant has not taught the artisan how to produce *any* opioid receptor encoded for by less than the full-length of SEQ ID NO:7 (claim 94). Claim 94 encompasses a process of screening a compound for its ability to bind to any opioid receptor, not just the mu opioid receptor. However, the only limitation in both independent claims 86 and 94 is that the opioid receptor must be encoded for by at least 35 contiguous bases of SEQ ID NO:7 and include the guanine at position 389 of SEQ ID NO:7. Based on this information, the requirements to produce a mu opioid receptor are exactly the same as to produce a non-mu opioid receptor. Therefore, given that the opioid receptor must comprise only as few as 11-33 amino acid resides of SEQ ID NO:8, the artisan is not able to distinguish between making a mu opioid receptor and making any other opioid receptor.

In summary, the breadth of the claims is excessive with regard to Applicants claiming a process for screening a candidate substance for its ability to bind to an opioid receptor encoded for by a nucleic acid molecule comprising only at least 35, 45, 50, 75, or 100 contiguous nucleotides of SEQ ID NO:7, including the guanine at position 389, as well as screening a candidate substance for its ability to bind to chimeric opioid receptors comprising said contiguous nucleotides. There is a lack of guidance and working examples of these nucleic acid molecules and proteins, as well as how to differentiate making mu opioid receptors from making non-mu opioid receptors. Applicants do not provide any language in the claims, or specification, which would allow the artisan to make a functional opioid receptor, either mu or non-mu opioid receptors by using as few as 35 contiguous bases of SEQ ID NO:7. The fact that the nucleic acid molecules encoding these receptors must comprise the guanine at position 389 of SEQ ID NO:7 is, itself, insufficient. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to differentially make a functional opioid receptor, as well as how to make both mu and

non-mu opioid receptors, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed. Claim 92 is rejected since it depends from rejected claim 86.

*8. Claim Rejections - 35 USC § 112, second paragraph*

A. The rejection of claim 44 under 35 USC 112, second paragraph, regarding the term "interact" has been withdrawn since this claim has been canceled and none of the new claims (83-101) recites "interact."

B. Claim 85 is confusing since it is not understood what is meant by the term "intrinsic activation ability." No definition of this term could be found in this large specification. Applicants are required to identify where in the specification this term appears.

C. Claims 86-90, 92, 93-99 and 101 are confusing since it is not clear in claims 86 and 94 if the guanine at position 389 of SEQ ID NO:7 is contained in the nucleic acid sequence comprising at least 35, 45, 50, 75 or 100 contiguous bases of SEQ ID NO:7, or is contained outside said sequence, but still in the same molecule. Claims 87-90, 92, 93, 95-99 and 101 are also rejected since they depend from these rejected claims.

*9. Claim Rejections - 35 USC § 102*

A. The rejection of claims 44-47, which correspond to new claims 83-85, under 35 USC 102(b), as being anticipated by Fukuda et al. (FEBS Letters 327:311-314, 1993) has been withdrawn in view of Applicant's statement on page 6 of the response, filed 2/26/02, that page 92 of U.S. Application Serial No. 08/305,518, which is a parent of the instant application, discloses SEQ ID NO:2 and that the invention of 08/305,518 also "contemplates a process of screening substances for their ability to interact with a mu opioid receptor polypeptide" (page 15 and Example II, on pages 78-79). Upon reviewing page 15 of parent application 08/305,518, as well as Example II which, in contrast to Applicant's statement that this is found on pages 78-79 of the parent application, is actually disclosed on pages 93-97, the Declaration is deemed persuasive by the Examiner.

To the extent that the Fukuda et al. (1993) reference is prior art under 35 USC 102(a), a Declaration under 37 C.F.R. 1.131 has been provided demonstrating that the Applicant was in possession of SEQ ID NO:2 and used this protein in binding studies at least as early as Fukuda et al. (1993). In this Declaration, the Applicant swears behind Chen et al. ("Chen" reference; Mol. Pharmacol. 44:8-12, 1993 –

see paragraph C of this section). Based on this, the Applicant states that swearing behind the Chen reference is evidence that the Applicant must have invented the aspect of the claimed invention and properly tested it at least as early as the date of submission of the Chen reference, May 4, 1993. This Chen reference is, therefore, evidence of invention of the claimed invention prior to the Fukuda et al. (1993) reference. Therefore, Fukuda et al. (1993) should not be prior art against the present application. These arguments are deemed to be persuasive by the Examiner and the rejection of claims 44-47, which correspond to new claims 83-85, under 35 USC 102, has been withdrawn.

B. The rejection of previous claims 65-68, 72, 74 and 76-78, which correspond to new claims 86-88, 92 and 94-97, under 35 USC 102(a) as being anticipated by Wang et al. (FEBS Letters 338:217-222, 1994) has been withdrawn in view of Applicant's arguments. The Applicant has argued that Wang et al. do not teach a recombinant opioid receptor encoded for by a polynucleotide which is at least 100 nucleotides in length and that includes the guanine nucleotide at position 389 of SEQ ID NO:7 of the present invention. Applicant also argues that line 2 of Figure 1 of the human sequence of Wang et al. has an asparagines at position 51 whereas the corresponding position of the protein of the present invention has an aspartate (SEQ ID NO:2 and pages 121, lines 20-25 of the instant specification). Finally, the Applicant argues that the GenBank Accession No. identified in the legend to Figure 1 of Wang et al. is L25119, which does not have a guanine at corresponding nucleotide position 389 of SEQ ID NO:7 of the present invention.

The Examiner agrees with the Applicant on all of these issues and has noticed that Sequence Comparisons B (which accompanied the Office Action dated 7/17/01) which shows that the sequence contained in GenBank Accession No. U12569 is, in fact, not that of Wang et al., but rather that of Bare et al. Both Bare et al. (FEBS Letters 354(2):213-216, 1994) and Wang et al. (FEBS Letters 338:217-222, 1994) can be seen on the paper entitled "Sequence Comparison B." The fact that the sequence shown in Sequence Comparison B is that of Bare et al. and not that of Wang et al. has been confirmed by the Examiner by a thorough review of the Wang et al. paper. Wang et al. only disclose one GenBank Accession No., L25119 (Figure 1, legend), and not GenBank Accession No. U12569, as seen on Sequence Comparison B of the Office Action dated 7/17/01.

In fact, a review of the amino acid "translation" on the first page of Sequence Comparison B and continuing to the first line of page 2 of Sequence Comparison B shows that the protein encoded for by that nucleic acid sequence is not the same as that taught in Figure 1 of Wang et al. This is most evident by comparing the C-terminal amino acid residues of both the "translated" protein of Sequence Comparison B

with that of Figure 1 of Wang et al. To further support this contradiction, the Applicant has provided a nucleotide printout of GenBank Accession No. L25119 in Appendix E of the response filed 2/26/02. This nucleotide sequence corresponds to that disclosed in the Wang et al. paper (Figure 1). It can be seen that this nucleotide sequence does not correspond to that of Sequence Comparison B. The nucleotide sequence provided by the Applicant in Appendix E of the response filed 2/26/02 is the correct sequence of Wang et al. Therefore, since the nucleotide sequence of Wang et al. (L25119) does not comprise the guanine residue at corresponding position 389 of SEQ ID NO:7 of the present invention, the nucleotide sequence (Sequence Comparison B) initially believed by the Examiner to be that of Wang et al. does not meet the limitations of the presently claimed invention.

To the extent that the amino acid sequence shown in Sequence Comparison C, also relied upon in the Office Action dated 7/17/01, would be prior art over claim 83-85 of the present invention, this is incorrect. Sequence Comparison C shows a protein which is 100% identical to SEQ ID NO:8 of the present invention, and also references Wang et al. However, as argued by the Applicant, and which can clearly be seen by comparing the amino acid sequence disclosed in Sequence Comparison C, with that of Wang et al., Sequence Comparison C is not that taught in Figure 1 of Wang et al. In comparing the amino acid sequence of Sequence Comparison C with that of Figure 1 of Wang et al. it can be seen that amino acid residue 51 of Sequence Comparison C is an asparagine (single letter abbreviation "N") whereas corresponding residue 51 of the protein of Wang et al. is an aspartate (single letter abbreviation "D"). Therefore, the protein shown in Sequence Comparison C, which references Wang et al., is, in fact, not the protein of Wang et al. Since Sequence Comparison C is 100% identical to SEQ ID NO:8 of the present invention, clearly the protein of Figure 1 of Wang et al. is not identical to SEQ ID NO:8 of the present invention and can, therefore, not be used as prior art against any claim of the present invention which recites SEQ ID NO:8.

Furthermore, to the extent that the Bare et al. reference (FEBS Letters 354(2):213-216, 1994) is prior art against any claim of the present invention, the Applicant has submitted a Declaration under 37 C.F.R. 1.131 stating that the Applicant cloned and sequenced the cDNA corresponding to SEQ ID NO:7, and encoding SEQ ID NO:8, at least as early as any July 24, 1994 submission to GenBank by Lane A. Bare. This Declaration has been considered and is deemed persuasive by the Examiner. Therefore, no rejection under 35 USC 102 over Bare et al. will be made.

C. Claims 83-85 are rejected under 35 USC 102(a) for the reasons already of record on pages 5-6 of the Office Action dated 7/17/01 regarding previous claims 44-47, as being anticipated by Chen et al. ("Chen" reference; Mol. Pharmacol. 44:8-12, 1993). First, the Examiner wishes to clarify that this previous rejection of claims 44-47 over Chen et al. was a rejection under 35 USC 102(a) and not under 35 USC 103(a) as the first line of the rejection states. The claims recite a process for screening a candidate substance for its ability to interact with a receptor of SEQ ID NO:2 and 4 by determining its binding affinity. Chen et al. teach nucleic acids which encode proteins which are 100% identical to SEQ ID NO:2 and 4 (Sequence Comparisons E and F of Paper No. 9). Chen et al. also teach methods of determining the ability of ligands to interact with this receptor ("Materials and Methods").

First, it is noted that this Declaration is a Katz Declaration should have been submitted under 37 C.F.R. 1.132 instead of 37 C.F.R. 1.131. However, this Declaration has been considered by the Examiner. The Declaration states that the present inventor, Lei Yu, was the only inventor of the claimed subject matter and that the co-authors, Yan Chen, Anton Mestek, Jian Liu and Joyce Hurley did not take part in the conception of any of the subject matter disclosed and claimed in the referenced patent application, and are, accordingly, not co-inventors of the patent application.

Yu further states that the concept of isolating, sequencing and characterizing the rat and human mu opioid receptors, and using such receptors in screening assays, which form the basis of the present application, was derived solely and independently by Yu and that the other co-authors of the Chen reference did not participate in the conception of the subject matter claimed in the present patent application. Based on this, it is concluded that Yu is the sole inventor co-author of the Chen reference since Yu invented the portions of the Chen reference that relate to the isolation and sequencing of the rat mu opioid receptor. However, Yu is drawing legal conclusions based on the information provided in the Declaration. In the Declaration under 37 C.F.R. 1.131 regarding the Chen reference, the Applicant stated that Yan Chen performed the library screening, DNA sequencing and some of the assays including binding studies with respect to a rat mu opioid receptor and Jian Liu also helped in performing the DNA sequencing of the rat mu opioid receptor clone and functional assays involving the clone. The Applicant also states that Joyce Hurley assisted with these functional assays. It appears, therefore, that at least these three co-authors were involved in the conception of the present invention since they were critical in its reduction to practice. This case is similar to that decided in *Amgen v.* Chugai, 18 USPQ 2d 1017(1991), wherein it was found that conception may not be achieved until reduction to practice in cases involving cloning genes. In this case, conception is the realization of the nucleotide sequence of SEQ ID NO:2 and

4, and that conception is not realized until these species have been isolated. Therefore, the Chen et al. reference represents prior art by another less than one year before the filing date of Yu.

*10. Claim Rejections - 35 USC § 103*

A. The rejection of claims 44-47, which correspond to new claims 83-85, under 35 USC 103(a), as being unpatentable over Fukuda et al. (FEBS Letters 343:42-46, 1994) in view of Fukuda et al. (FEBS Letters 327:311-314, 1993), has been withdrawn in view of the submission of a Declaration under 37 C.F.R. 1.131 demonstrating that the Applicant was in possession of the polypeptide of SEQ ID NO:17 prior to the April 18, 1994 publication date of Fukuda et al. (FEBS Letters 343:42-46, 1994). This Declaration has been reviewed and is deemed to be persuasive by the Examiner. The Examiner wishes to clarify, in the first paragraph of the rejection under 35 USC 103(a) on page 6 of this Office Action dated 7/17/01, that SEQ ID NO:17 should have been the only SEQ ID NO referred to in the rejection and that "SEQ ID NO:2" should have then read' SEQ ID NO:17." However, this issue was not addressed by the Applicant and did not have any affect on the persuasiveness of the Declaration under 37 C.F.R. 1.131.

*11. Conclusion*

A. Claims 91 and 100 are objected to for the reasons set forth in the above section entitled "Claim Objections," but would be allowable if rewritten in independent format to include all the limitations of the base claims and to obviate the objections of their current base claims, from which they depend.

*Advisory information*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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May 27, 2002

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